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Cardiogenic shock complicating myocardial infarction: a lost cause or reasons for hope?

Choc cardiogénique de l'infarctus du myocarde : cause perdue ou raisons d'espérer ?

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Cardiogenic shock is still by far the leading cause of mortality during the acute phase of myocardial infarction. There has only been a very slight fall in its incidence of nearly 6% in patients hospitalized for infarction. However, its prognosis has improved during the last decade following the more widespread use of emergency revascularization by primary angioplasty, with a reduction of in-hospital mortality from 60-65% in 1995 to 45-50% today [1]. In particular, patients surviving the hospital phase may now hope for an excellent prognosis and good long-term quality of life [2, 3]. This combination of still unacceptable early mortality and the prospect of good long-term prognosis for survivors should therefore encourage "maximalist" management during the acute phase. In this edition, Samadi et al. show that in-hospital and 6-months mortality remain catastrophic (70 and 78% respectively) in patients aged over 75 years hospitalized for myocardial infarction complicated by cardiogenic shock, despite optimal revascularization by primary angioplasty with intra-aortic balloon counterpulsation [4]. This result is explainable but disappointing. Explainable, as it has been clearly shown that cardiogenic shock and age are by far the 2 most powerful predictors of post-infarction mortality. Explainable also by the mitigated results obtained when this strategy was systematically used to manage elderly subjects in the SHOCK study (SHould we emergently revascularize Occluded coronary arteries for Cardiogenic shocK), raising the question of the selection of patients who may benefit from this procedure in this age range [5]. However, these results are disappointing , as progress in angioplasty made since the SHOCK study, with the systematic use of stents and the improvement in the anti-thrombotic environment, has raised hopes that revascularization and its subsequent prognosis would be improved. Disappointing also because of the high-quality multidisciplinary management that these patients certainly received, in a reference institution grouping all the essential skills required to treat serious cardiovascular diseases. These results should not lead to discouragement, and as pointed out by the authors in their conclusion, they should persuade us "to evaluate the respective place of surgical revascularization and circulatory support".

In shock after myocardial infarction, the best revascularization strategy has not been clearly determined for multivessel coronary disease, which was the case for nearly 90% of the patients in the SHOCK study. In certain cases, coronary anatomy lends itself better to surgery than to angioplasty, and angioplasty of arteries not responsible for the infarct may be hazardous under such unstable hemodynamic conditions. In the SHOCK study, despite the more severe clinical and angiographic characteristics (three-vessel or left main trunk disease, diabetes etc.), the patients treated by surgical revascularization had an identical survival and quality of life as patients treated by angioplasty [6]. Recent data of the Society of Thoracic Surgeons National Cardiac Database indicate an operative mortality of 20% for surgical revascularization after infarction complicated by shock , and 33% when revascularization is associated with heart valve surgery [7]. Today, emergency bypass surgery is too rarely considered. If it is used more often in appropriate cases, and thanks to recent progress (beating-heart techniques, systematic use of the internal mammary artery, etc.) contemporary cardiac surgery would permit a substantial improvement in the prognosis of these patients. The other promising avenue of investigation is circulatory support. In theory, temporary left ventricular assist support is the

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ideal way of stopping the ischemia-hypotension-myocardial dysfunction spiral, permit recovery from ventricular stunning and await the disappearance of neurohormonal disturbances. This approach is restricted in practice by the complications of current devices and irreversible ventricular lesions [8].

Schematically, circulatory support may be used in 3 different manners.

- As a bridge to recovery. In this case, percutaneous extracorporeal assist devices, such as the ECMO (Extra-Corporeal Membrane Oxygenator), TandemHeart™ or Impella™ systems, are used. This approach remains disappointing. Current data, including 2 randomized TandemHeart vs intra-aortic balloon pump studies [9, 10], suggest that, despite the hemodynamic improvement in the mechanical support group, hospital mortality was not decreased because of the secondary occurrence of multiorgan failure.
- As a bridge to transplantation. In this case, percutaneous and then surgically implanted assist devices, are used sequentially ("Bridge to bridge"). In the largest series reported to date, involving 49 patients, 74% survived transplantation and 87% of transplant recipients survived beyond the hospital phase [11]. The Rouen series, recently published in this journal, also shows the feasibility of such an approach, with encouraging results [12]. However, the shortage of organs and the large number of patients who, in this context, are not candidates for transplantation – in particular elderly subjects – are major obstacles to its widespread use.
- It is therefore possible that the most promising solution for the future is, for many patients, the implantation of an indwelling LVAD [12, 13]. In addition to currently unresolved technical issues, it will then be necessary *to precisely define selection criteria* of candidates according to strict clinical parameters, irreproachable ethical rules, within the framework of rigorous economic constraints.

A final, inflammatory, peripheral vascular and neurohormonal approach should be mentioned. Cardiogenic shock during myocardial infarction causes a systemic inflammatory response syndrome [SIRS] responsible among other things for inappropriate peripheral vasodilatation [14]. A large rise in cytokine levels then rapidly occurs. Tumor Necrosis Factor-d and interleukin-6 have a myocardial depressant effect. Complement is also involved in SIRS. Despite an encouraging phase 2 study , a trial on the inhibition of complement C5 by pexelizumab did not show an effect either on the occurrence or mortality of cardiogenic shock [14]. However the most interesting avenue of research concerns NO. Serious infarction causes an increase in the expression of inducible NO synthase, leading to excessively high NO levels, responsible for vasodilatation, myocardial depression and interference with the action of catecholamines. Although the randomized study TRIUMPH (Tilarginine Acetate Injection in a Randomized International Study in Unstable MI Patients with Cardiogenic Shock) was negative [15], this approach has not been abandoned and other studies will be necessary to definitively confirm the role of SIRS and inducible NO synthase in the prevention and treatment of post-infarction cardiogenic shock.

Cardiogenic shock which is responsible for 60% of deaths during the acute phase of myocardial infarction is still the main target disorder for therapy to substantially improve prognosis. During the last decade, an improved use of resources has made it possible to obtain a definite reduction in mortality, thanks to primary angioplasty with intra-aortic balloon pumping. It is therefore necessary to continue this approach and encourage increasingly invasive management of serious infarcts. However, the study by Samadi et al. [4] shows that, even when it is conducted under the best possible conditions, percutaneous revascularization remains ineffective in many patients, and, in particular, in elderly subjects. The improvement in the prognosis of cardiogenic shock therefore requires the implementation of other revascularization strategies, the development of circulatory support and the investigation of new medications. Cardiogenic shock should then no longer be a lost cause for many patients, but a curable disorder with a reasonable chance of recovery. There are still therefore reasons to hope… though it should always be born in mind that the best treatment will be always preventive, by effective and early reperfusion during the acute phase of infarction.

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